REMARKS

This Amendment is submitted in reply to the non-final Office action mailed on February 1, 2010 The Office Action provided a three-month shortened statutory period in which to respond, ending on May 1, 2010. Accordingly, this amendment is timely submitted. No fees are believed due with this Amendment. The Director is authorized to charge any fees that may be required, or to credit any overpayment to Deposit Account No. 50-4498 in the name of Nestle Nutrition.

Claims 1-4, 6-14 and 16-28 are currently pending. Claims 6, 12 and 18-22 were previously withdrawn. Claims 5, 15 and 29 were previously canceled. In the Office Action, Claims 10, 13-14, 16 and 26 are rejected under 35 U.S.C. §112. Claims 1-4, 7-11, 13-14, 16 and 23-26 are rejected under 35 U.S.C. §102, and Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are rejected under 35 U.S.C. §103.

In response Claims 1-3, 10, 13-14, 17, 23-26 and 28 have been amended. The amendments do not add new matter and are supported in the specification at, for example, page 2, lines 23-30; page 4, lines 5-15. In view of the amendments and/or for the reasons set forth below, Applicant respectfully submits that the rejections should be withdrawn.

In the Office Action, Claims 10, 13-14, 16 and 26 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Patent Office states that Claims 10, 13-14, 16 and 26 recite the phrase "per serving or . . . per daily dose" and that it is "unclear how one can quantify the amount of a component in a daily dose." See, Office Action, page 29, line 21-page 30, line 13. In response, Applicant has amended Claims 10, 13-14 and 26 to delete the word "daily." The amendment is solely for clarification purposes and not to avoid and prior art. Applicant submits that the skilled artisan would immediately understand the scope of the present claims when read in view of the specification.

For example, the specification clearly explains that one dose (per day, for example) may be comprised of several servings, or may be one dose containing as much effective ingredients as the total of the several servings. Indeed, the specification states that the "daily dose of e.g. about 15 g essential amino acids, e.g., in free and/or salt form, may be given 3 times per day, e.g. in 3 servings of about 5 g, with equal effectiveness." See, specification, page 10, line 20-page 11,

line 4. The specification also states that "[a] suitable serving size may be in the range of about 20 to about 500 ml" and "[t]he compositions of the invention may provide benefit with as few as for example two servings per day." See, specification at, for example, page 11, lines 21-22. As such, it is clear that a "serving" is a smaller portion than a "dose," but that each quantity can require certain amounts of ingredients. Accordingly, the skilled artisan would immediately appreciate the scope of Claims 10, 13-14, 16 and 26 when read in view of the specification.

For at least the reasons set forth above, Applicant respectfully submits that Claims 10, 13-14, 16 and 26 fully comply with the requirements under 35 U.S.C. §112, second paragraph.

Accordingly Applicant respectfully requests that the rejection of Claims 10, 13-14, 16 and 26 are rejected under 35 U.S.C. §112, second paragraph, be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 7-11, 13-14, 16 and 23-26 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,077,828 to Abbruzzese, et al. ("*Abbruzzese I*"). Claims 1-4, 7-11, 13-14, 16 and 23-26 are rejected under 35 U.S.C. §102(a) as being anticipated by U.S. Patent No. 6,387,883 to Abbruzzese, et al. ("*Abbruzzese II*"). Applicant respectfully submits that *Abbruzzese I* and *Abbruzzese II* are deficient with respect to the present claims.

Currently amended independent Claims 1-2 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least 30% to about 95% by weight based on the weight of total amino acids. Currently amended independent Claims 23-24 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least 30% by weight based on the weight of total amino acids. Currently amended independent Claims 3, 17, 25 and 28 recite, in part, leucine, in free and/or salt form, is present in an amount of at least 30% by weight based on the weight of intact protein. Currently amended independent Claims 1-3, 17, 25 and 28 also recite, in part, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 and wherein the ratio of leucine in free and/or salt form to leucine in form of the intact protein is about 3:1 to about 1:3. The amendments do not add new matter and are supported in the specification at, for example, page 2, lines 23-30; page 4, lines 5-15.

Applicant has found that when dietary intake is limited below the optimal level for physiological or patho-physiological reasons, a dietary supplement must be more effective than normal food intake in order to provide a benefit. This is because in this circumstance, when a

dietary supplement is given, normal food intake is likely to be reduced by a calorically equivalent amount. Consequently, a supplement designed to limit cancer cachexia, for example, should stimulate muscle protein synthesis to a greater extent than normal food intake and should not interfere with the response to meal intake. Trials of conventional nutritional supplements in patients with cancer cachexia have failed to show appreciable benefit in terms of weight gain or quality of life. Accordingly, there is a need for effective nutritional approaches capable of treating, preventing or ameliorating the effects of tumor-induced weight loss due to, for example, cancer cachexia and/or anorexia.

Applicant has surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein alone is optimal. See specification, Examples 1-2. Applicant has also found that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that has particularly high amounts of leucine had a stimulatory effect on muscle protein synthesis. See specification, Example 3.

In addition, Applicant has surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight loss, such as cachexia, e.g. cancer cachexia, may be obtained by combining essential amino acids in free form and/or in salt form with intact protein. See specification, Example 2. The effect of such a combination is greater than the effect that can be achieved with either type of combination partner alone. In contrast, Applicant respectfully submits that the cited references fail to disclose or suggest every element of the present claims.

Abbruzzese I and *II* both fail to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least 30% by weight based on the total amino acids or weight of intact protein as required by the present independent claims. The Patent Office admits same. See, e.g., Office Action, page 4, lines 7-10. *Abbruzzese I* and *II* also fail to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90, and wherein the ratio of leucine in free and/or salt form to leucine in form of the intact protein is about 3:1 to about 1:3 as required by independent Claims 3 and 25.

In the Office Action, the Patent Office performs a calculation based on amounts of branched-chain amino acids in an alleged composition and an amount of leucine in the branched-chain amino acids to imply that there is at least about 23% of leucine in the composition. See, e.g., Office Action, pages 4, 9 and 11-12. However, Applicant respectfully submits that this calculation is misguided.

For example, the portion of *Abbruzzese II* cited by the Patent Office states that "[t]he total amount of branched-chain amino acids ("BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e., percent), preferably about 15-25 g/100 g. Thus, an 8 oz container of the nutritional composition would contain up to about 8 g BCAAs per 16 grams of total protein. The daily delivery of BCAAs is about 5-26 g." See, *Abbruzzese II*, column 9, lines 26-31. However, this calculation does not consider that the compositions of *Abbruzzese I* and *II* require a certain amount of a "source of amino-nitrogen," wherein 15-50% by weight of the amino-nitrogen is branched-chain amino acids. See, e.g., *Abbruzzese II*, column 3, line 58-column 4, line 5; column 4, lines 29-33. Therefore, if the compositions of *Abbruzzese I* and *II* require a lower amount of a source of amino-nitrogen, the compositions of *Abbruzzese I* and *II* will have a lower amount of leucine. Accordingly, the portion of the reference cited by the Patent Office is not necessarily the amount of branched-chain amino acids in the entire composition, but rather, the amount of branched-chain amino acids in the source of amino-nitrogen.

Further, Applicant notes that the Patent Office's calculations explicitly states that "[s]ince the reference teaches that the total amount of BCAA useful in the present invention is about 15-50 g/100 g protein, and there is 46% of leucine in the BCAA composition, this implies that there is at least about 23% leucine." Applicant disagrees and submits that the calculation implies that there is at most 23 % leucine and as little as 6.9 % leucine. Accordingly, Applicant submits that the at most 23% leucine of both *Abbruzzese I* and *II* is very different from the at least 30% leucine required, in part, by the present claims. Thus, even assuming that the Patent Office's calculation is correct, which Applicant does not believe, the Patent Office's calculation assumes the upper-most range of leucine available in the composition. In other words, in a composition comprising 15-50 g/100 g protein of branched-chain amino acids, the Patent Office's calculation assumes 50 g/100 g protein (i.e., 50%) to arrive at an implied amount of 23% leucine. As is

inherently admitted by the use of the greatest amount of branched-chain amino acids, the compositions of *Abbruzzese I* and *II* cannot contain more than about 23% leucine.

The Patent Office even admits that "claims 1-3 and 23-25 have been rejected over the prior art, even though the reference does not disclose exact % range as claimed. However, both the claims and the reference utilize the term 'about' when discussing the amount of leucine." See, Office Action, page 4, lines 7-10 (emphasis added). Applicant notes that, by definition, the present rejections of Claims 1-4, 7-11, 13-14, 16 and 23-26 as being anticipated under 35 U.S.C. §102 cannot stand since the Patent Office admits that the references do not teach each and every element of the present claims.

The Patent Office attempts to remedy the lack of disclosure of the claimed ranges by stating that "the disclosure of leucine in about 23% encompasses a % of 'about' 25%, as claimed." See, Office Action, page 4, lines 20-21. Applicant disagrees for at least the following reasons. Initially, Applicants note that the claims were previously amended to recite "about 30% leucine" instead of "about 25% leucine." Further, in view of a 2007 opinion, in which the Federal Circuit stated that the term "about" must be interpreted in its technological and stylistic context," Applicant submits that the skilled artisan would recognize a composition having about 23% leucine would be entirely distinguishable from a composition having about 30% leucine, as is required, in part, by the present claims. See, *Ortho-McNeil Pharmaceutical, Inc. v. Caraco Pharmaceutical Labs, Ltd.*, 476 F.3d 1321, 1326 (Fed. Cir. 2007).

Regardless, Applicant notes that independent Claims 1, 2,3, 17, 23-25 and 28 have been amended to recite, in part, compositions including "at least 30% leucine." The amendments do not add new matter and are supported in the specification at, for example, page 2, lines 23-30. Accordingly, the present claims now require "at least 30% leucine," which is not disclosed by either *Abbruzzese I* or *Abbruzzese II*, as is admitted by the Patent Office.

Abbruzzese I and *II* also fail to disclose or suggest wherein the ratio of leucine in free and/or salt form to leucine in form of the intact protein is about 3:1 to about 1:3 as required by independent Claims 3 and 25. Indeed, *Abbruzzese I* and *II* fail to even disclose or suggest leucine in free and/or salt form and leucine in form of intact protein, let alone wherein the presently claimed ratio of the two.

Instead, since both *Abbruzzese I* and *II* share the same specification, both of the references are directed to methods and nutritional compositions for preventing and treating cachexia and anorexia. The compositions of *Abbruzzese I* and *II* includes effective amounts of (1) ω3 fatty acids, such as α-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid or mixtures thereof; (2) branched-chain amino acids, such as valine, leucine, isoleucine or mixtures thereof; with or without reduced levels of tryptophan and 5-hydroxytryptophan; and (3) an anti-oxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium, or mixtures thereof. See, e.g., *Abbruzzese II*, column 3, lines 15-56.

In the only example that utilizes leucine, *Abbruzzese I* and *II* teach an amino acid profile for his nutritional composition with leucine in an amount of 9.08 g/100 g protein (i.e. 9.08%), which is substantially lower than that of the present claims. See, e.g., *Abbruzzese II*, column 9, line 17. Moreover, in the compositions of *Abbruzzese I* and *II*, the ratio of total essential amino acids and conditionally essential amino acids to total amino acids is 0.51, which is also much lower than that of the present claims.

Further, anticipation is a factual determination that "requires the presence in a single prior art disclosure of each and every element of a claimed invention." *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747 (Fed. Cir. 1987) (emphasis added). Federal Circuit decisions have repeatedly emphasized the notion that anticipation cannot be found where less than all elements of a claimed invention are set forth in a reference. See, *e.g.*, *Transclean Corp. v. Bridgewood Services, Inc.*, 290 F.3d 1364, 1370 (Fed. Cir. 2002). As such, a reference must clearly disclose each and every limitation of the claimed invention before anticipation may be found. In the instant case, the Patent Office has failed to identify any disclosure in either *Abbruzzese I* or *Abbruzzese II* that demonstrates that composition require at least 30% leucine as is required, in part, by the present claims. Instead, the Patent Office must be able to specifically identify the disclosure of each and every limitation of the claimed invention before anticipation may be found.

For at least these reasons, Applicant respectfully submits that the anticipation rejections are improper and that *Abbruzzese I* and *Abbruzzese II* fail to anticipate the presently claimed subject matter.

Accordingly, Applicant respectfully requests that the anticipation rejections of Claims 1-4, 7-11, 13-14, 16 and 23-26 under 35 U.S.C. §102 be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Abbruzzese I* in view of U.S. Patent No. 6,420,342 to Hageman, et al. ("*Hageman*") and U.S. Patent No. 6,953,679 to Salvati, et al. ("*Salvati*"). Claims 1-4, 7-11, 13-14, 16-17 and 23-26 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Abbruzzese I* in view of U.S. Publication No. 2003/0119888 to Allen et al. ("*Allen*") and Sports Supplement Review, 1997, pp. 66-70 to Phillips Bill ("*Phillips*"). Applicant respectfully disagrees with and traverses these rejections for at least the reasons set forth below.

Hageman, Salvati, Allen and *Phillips* fail to remedy the deficiencies of *Abbruzzese I.* For example, *Hageman, Salvati, Allen* and *Phillips* fail to disclose or suggest leucine, in free and/or salt form, is present in an amount of at least 30% by weight based on the total amino acids or the weight of intact protein as required by the present claims. *Hageman, Salvati, Allen* and *Phillips* also fail to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claims 3, 17, 25 and 28. *Hageman, Salvati, Allen* and *Phillips* also fail to disclose or suggest wherein the ratio of leucine in free and/or salt form to leucine in form of the intact protein is about 3:1 to about 1:3 as required by independent Claims 3, 17, 25 and 28.

Hageman generally describes a nutritional, pharmaceutical or dietetic preparation that includes effective amounts of ribose and folic acid, optionally combined with other components, such as niacin, histidine, glutamine, orotate, vitamin B6 and other components. See *Hageman*, column 5, lines 8-52. *Hageman* also discloses products having the following mixture of amino acids as beneficial for muscle growth when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt % histidine, 5-15 wt % isoleucine, 10-23 wt % leucine, 10-23 wt % lysine, 515 wt % methionine, 5-15 wt % phenylalanine, 5-15 wt % threonine. See *Hageman*, column 6, line 62-column 7, line 1. The maximum level of leucine of *Hageman's* composition is 23%, which is lower than that of the present claims.

Salvati generally describes fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders and pharmaceutical compositions containing such compounds. See *Salvati*, Abstract. *Salvati*, along with *Hageman*, lists leucine as one of many amino acids and fails to recognize or suggest any superior benefit from increased levels of leucine beyond what is taught. Consequently, the skilled artisan would have no reason to optimize the leucine range of *Hageman* and *Salvati* in accordance with that of the present claims in the absence of hindsight.

Allen is entirely directed to a composition for stimulating muscle growth having an effective amount of L-arginine. See, *Allen*, Abstract. As shown by Example 1 of *Allen*, a preferred composition of the invention included about 0.57% leucine. Further, *Phillips* is cited solely for the teaching that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of leucine and may help to build muscle. See, Office Action, page 36, lines 4-8. However, *Phillips* fails to remedy the deficiencies of *Abbruzzese I, Hageman, Salvati*, and *Allen*.

The Patent Office asserts that finding the optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids would have been obvious to the skilled artisan in view of *Hageman* and *Salvati* teachings. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Patent Office. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Applicant respectfully submits that there is absolutely no guidance in *Hageman* and *Salvati* for one of skill in the art to choose the active components and effective amount of the components present in the instant claims to achieve the unexpectedly improved composition as Applicant has done. To arrive at the claimed optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids in accordance with the present claims, the skilled artisan would have to select these specific components from the numerous components taught by *Hageman* and *Salvati*. *Hageman* teaches the use of ribose, folate, magnesium, niacin, selenium, thiamine, glucose, citrate, histidine, phosphate, sulfate and

vitamin B12 and numerous amino acids as active components in his composition. See *Hageman*, columns 5-6. *Salvati* teaches thousands of possible fused cyclic compounds that can be part of his nutritional composition along with whey protein or casin, amino acids, triglycerides, vitamins, minerals, carnitine, lipoic acid, creatine, and coenzyme Q-10. See *Salvati*, columns 3-8.

The skilled artisan would have to perform an undue amount of experimentation based on the thousands of individual compounds listed by *Hageman* and *Salvati* to arrive at the specific components and ranges recited by the present claims. The sheer quantity of experimentation necessary to arrive at the composition would be excessive. Moreover, *Hageman* and *Salvati* do not provide any direction or guidance for using leucine over any other amino acid, and there would be thousands of combinations that would not include any of leucine. As a result, there is no reason that the skilled artisan would optimize the leucine range or amino acid ratios of *Hageman* and *Salvati* in accordance with that of the present claims.

Applicant also respectfully submits that the skilled artisan would not arrive at the claimed invention using *Hageman* and *Salvati* in the absence of hindsight because the cited references are entirely directed to compositions utilizing different nutritional ingredients for different intended purposes. Moreover, *Hageman* and *Salvati* fail to even recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Applicant respectfully submits that the Patent Office is using Applicant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Hageman* and *Salvati*. *Allen* and *Phillips* fail to remedy such deficiencies.

For at least the above-mentioned reasons, Applicant respectfully submits that the present claims are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

Accordingly, Applicant respectfully requests that the obviousness rejections of Claims 1-4, 7-11, 13-14, 16-17 and 23-28 be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 7-11, 13-14, 16-17 and 23-27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-3 and 5-11 of copending U.S. Application No. 12/110,016, and as being unpatentable

over Claims 1-2, 5 and 7 of copending U.S. Application No. 12/366,520. In response, Applicant submits that the present claims have been amended to include additional limitations not previously recited. Accordingly, since the scope of the present claims, or the claims of copending U.S. Application No. 12/366,520, may further change during prosecution, Applicant submits that it is premature to argue against, or submit a terminal disclaimer to overcome, the double patenting rejections.

Accordingly, Applicant respectfully requests that the provisional rejections of Claims 1-4, 7-11, 13-14, 16-17 and 23-27 under obviousness-type double patenting be reconsidered and withdrawn.

For the foregoing reasons, Applicant respectfully requests reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims that could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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